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EXAMINER	
KARPINSKI, LUKE E	

ART UNIT	PAPER NUMBER
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/822,627	XIE ET AL.	
	Examiner	Art Unit	
	LUKE E. KARPINSKI	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-17 and 20-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-17, and 20-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Amendments to the Claims and Remarks filed 12/19/2007 is acknowledged.

Claims 1, 4-17, and 20-24 are currently pending.

Claims 2, 3, 18, 19, and 25-33 have been canceled by the Applicant.

Withdrawn Claim Rejections - 35 USC § 103

The rejection of claims 1-33 under 103, as being unpatentable over US Patent No. 5,478,577 to Sackler et al. in view of US Patent No. 6,372,255 to Saslawski et al. is hereby withdrawn in light of the amendment filed 12/19/2007.

Response to Arguments

Applicant's arguments with respect to claims 1-33 have been considered but are moot in view of the new ground(s) of rejection which are necessitated by amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-17, and 20-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Applicant has amended claim 1 to read "and (d) optionally a cosmetic coating wherein the pH dependent material consists of a first enteric..." It is not understood if the Applicant claims the pH dependant material in the cosmetic coating or if the limitations refer to component (b), subcomponent (i) in instant claim 1. It is also not understood if the Applicant is claiming a pH dependent material which has more than one coating or more than one enteric agent, see last 4 lines of amended claim 1 filed 12/19/2007. Therefore the metes and bounds of the claims are vague and indefinite. Thus claims 1, 4-17, and 20-24 are rejected under 35 USC 112.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.

3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 1, 4-17, and 20-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 5,160,742 to Mazer et al. in view of US Patent No. 6,372,255 to Saslawski et al. and US Patent No. 5,478,577 to Sackler et al.

Applicant Claims

Applicant claims an oral pharmaceutical comprising: (a) a core comprising: oxycodone or a salt thereof; at least one excipient; and (b) a delayed release coating consisting essentially of: (i) a pH dependant material; (ii) an inert processing aid and; (iii) optionally a plasticizer and; (c) an immediate release drug layer comprising: (i) oxycodone or a salt thereof; (ii) a binder; and (d) optionally a cosmetic coating. The

Applicant further claims specific types and compounds as excipients, viscosities, pH dissolution values, ratios and, percentages.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Mazer et al. teach a formulation comprising: (a) a core comprising an analgesic (col. 6, lines 65-68) and at least one excipient (col. 7, lines 11-45); and (b) a delayed release coating consisting essentially of: 30-80% of a pH dependant material (Eudragit) (col. 8, lines 39-42 and col. 11, lines 13-21), about 20-70% of an inert processing aid (talc); and a plasticizer (acetyltri-n-butyl citrate) (col. 8, lines 43-51). Mazer et al. also teach about 35-70% of a pH dependant material (Eudragit) (col. 11, lines 13-21). The percentage of Eudragit present is extrapolated from the second coating material taught in col. 11, lines 13-21, the coating material comprises 15% plasticizer and 30% processing aid, the only other ingredient named is the pH dependant material, which means that the pH dependant material is present at 45%. Mazer et al. also teach a pH dependant material consisting of a first enteric agent that begins to dissolve or degrade at a pH of about 5 to 7 (Eudragit L100) and a second enteric agent that begins to dissolve at a pH of above 7 (Eudragit S100) (col. 8, lines 39-42), as evidenced by the "Handbook of Pharmaceutical Excipients" pages that were provided by the Applicant in the Arguments/Remarks filed 12/19/2007 It is noted by the Examiner that enteric coatings necessarily degrade in the intestinal tract. Mazer et al. also teach that said enteric agents are found at a ratio between 1:5 and 5:1 (col. 8, lines 39-42). Mazer et al. also teach said core comprising a binder (col. 7, lines 11-15), a diluent (dextrose)

(col. 7, lines 11-26), a glidant and a lubricant (lactose) (col. 7, lines 11-25). Mazer et al. further teach an osmopolymer (polyvinylpyrrolidone) as said binder (col. 7, lines15-30).

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

1. Mazer et al. do not teach an immediate release drug layer. This deficiency in Mazer et al. is cured by Saslawski et al. Saslawski et al. teach an immediate release drug layer comprising an analgesic or a salt thereof (col. 2, lines 54-56) and at least one excipient (col. 5, lines 59-67), said immediate release drug layer covering a sustained release drug layer (abstract). Saslawski et al. also teach the benefit of instant bioavailability and optimization of the supply of the active (col. 1, lines 6-50). Further, Mazer et al. do not teach said binder having a viscosity of greater than 50,000 or 75,000 mPa when tested in a 2% aqueous solution at 20ºC as claimed in claims 17 and 20. This deficiency is cured by Saslawski et al. Saslawski et al. teach binders utilized in the core, particularly hydroxypropylmethylcellulose (col. 6, lines 56-65). It is noted that in Saslawski et al. the prolonged release layer and the core are one in the same. It is also noted that hydroxypropylmethylcellulose has all of the claimed properties as stated by the Applicant in the instant specification. Further, Mazer et al. do not teach the enteric agents present at a ratio from about 1:2 to 1:4 as claimed in claim14. However, Mazer et al. do teach a ratio of 3:1 and that each enteric agent has different dissolution at designated pH levels. Further, Mazer et al. do not teach a single coating comprising enteric agents that begin to dissolve at a pH of above 9 or 11-12 as claimed in claims

12, 21, and 22. However, Mazer et al. do teach a separate coating comprising zein, as well as the fact that coatings comprising zein lower the amount of active released due to simulated gastric fluids (col. 15, lines 23-50 and figure 1).

2. Neither Mazer et al. nor Saslawski et al. teach the utilization of oxycodone. This deficiency is cured by Sackler et al. Sackler et al. teach that oxycodone is an angesic capable of use in the sustained release layer and immediate release layer of a pharmaceutical formulation (col. 6, line 24 to col. 7, line 10).

Finding of Prima Facie Obviousness Rational and Motivation

(MPEP §2142-2143)

1. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to coat the sustained release drug formulation of Mazer et al. with an immediate release drug layer comprising: an analgesic active and an excipient, as taught by Saslawski et al. in order to produce the invention of instant claims 1 and 17.

One of ordinary skill in the art would have been motivated to do this because Mazer et al. teach sustained release drugs and Saslawski et al. teach that covering sustained release drugs with an immediate release layer ensures instant bioavailability followed by a sustained release period, as well as, the fact that formulations with such layers make it possible to optimize the supply of active ingredients in the body. Therefore it would have been obvious to utilize the immediate release layer of

Saslawski et al. comprising: an analgesic active and an excipient, with the formulations of Mazer et al. in order to provide instant bioavailability of an active followed by prolonged release of said active.

2. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to utilize oxycodone as an active in the sustained release drug formulations of Mazer et al. covered with an immediate release drug layer comprising: oxycodone and an excipient, as taught by Saslawski et al. in order to produce the invention of instant claims 1 and 17.

One of ordinary skill in the art would have been motivated to do this because Mazer et al. teach the sustained release layer comprising an analgesic and Saslawski et al. teach an immediate release layer comprising an analgesic. Sackler et al. teach a formulation comprising oxycodone, as an analgesic, within both an immediate release layer and a sustained release layer of a pharmaceutical formulation. The criticality of the formulations of Mazer et al. and Saslawski et al. lies in the release of an active agent not in the active agent itself. Therefore it would have been obvious to utilize oxycodone as one analgesic of choice in both the sustained release compositions of Mazer et al. and the immediate release compositions of Saslawski et al. in order to provide immediate and prolonged pain relief.

Regarding claim 8, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to utilize hydroxypropylmethylcellulose in the core formulations of Mazer et al. as taught by Saslawski et al.

One of ordinary skill in the art would have been motivated to do this because Mazer et al. teach a pharmaceutical core formulation comprising: an active in a matrix with a binder. Saslawski et al. teach hydroxypropylmethylcellulose as a binder used in pharmaceuticals. Saslawski et al. teach only 6 different examples of binders, with such a limited number taught it would have been reasonable for one of ordinary skill to try all of the binders taught by Saslawski et al. Therefore it would have been obvious to utilize hydroxypropylmethylcellulose in the formulations of Mazer et al. as a binder.

Regarding claim 14, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to utilize a ratio of a first enteric agent and a second enteric agent from about 1:2 to 1:4 in the formulations of Mazer et al.

One of ordinary skill in the art would have been motivated to do this because Mazer et al. teach a ratio of 3:1 and that each enteric agent has different dissolution properties at designated pH levels. Therefore it would have been obvious to modify the enteric agent ratio in order to release more or less active in different sections of the gastrointestinal tract.

Regarding claims 11, 12, 21, and 22, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to utilize zein and another enteric agent in a single sustained release layer in the formulations of Mazer et al.

One of ordinary skill in the art would have been motivated to do this because Mazer et al. teach that zein and other enteric agents, in combination, reduce the amount of active released in the stomach and regulate the release within the intestines. One

would also be motivated to combine the zein and another enteric agent into a single coating to reduce the number of processing steps during manufacture. Therefore, it would have been obvious to use zein and another enteric agent (Eudragit) in a single coating to speed up manufacture and to produce a formulation which reduces active agent release in the stomach and provides targeted release in different areas of the intestine.

From the teachings of the reference, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Thus instant claims 1, 4-17, and 20-24 are deemed to be obvious by Mazer et al. in view of Saslawski et al. and Sackler et al.

Conclusion

Claims 2, 3, 18, 19, and 25-33 have been canceled by the Applicant.

Claims 1, 4-17, and 20-24 are rejected.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Inquiries

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LUKE E. KARPINSKI whose telephone number is (571)270-3501. The examiner can normally be reached on Monday Thursday 9-4 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LEK

/Sharmila Gollamudi Landau/

Primary Examiner, Art Unit 1611